Remarks

This Amendment responds to the final Office Action mailed on January 20, 2006. In the final Office Action, the Examiner rejected claims 21 and 23-34 in this application. Applicants respectfully submit that all of the pending claims are allowable for at least the following reasons.

The Rejection of Claims Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-4 of the Office Action, claims 21 and 23-28 are rejected as allegedly obvious over WO 92/00103 by Johnson ("the '103 publication"), in view of U.S. Patent No. 5,712,302 to Young ("the '302 patent"). In particular, it is alleged that the claims are obvious because: 1) the '103 publication discloses a combination of a 5-HT_3 antagonist and a 5-HT reuptake inhibitor, and racemic ondansetron and fluoxetine are disclosed as a 5-HT_3 antagonist and a 5-HT reuptake inhibitor, respectively; and 2) the '302 patent discloses that R(+) ondansetron decreases adverse effects associated with racemic ondansetron. (Office Action, pages 3-4). Applicants respectfully disagree.

It appears that the rejection is based on the Examiner's allegation that the following two steps are obvious: 1) selecting the combination of ondansetron and fluoxetine based on the '103 publication's disclosure; and 2) replacing ondansetron with R(+) ondansetron in so selected combination, based on the '302 patent's disclosure. Applicants respectfully point out that neither step is obvious for at least the following reasons.

First, Applicants respectfully submit that the references cited by the Examiner cannot render the specific combination of ondansetron and fluoxetine obvious. Applicants respectfully point out that while the '103 publication discloses racemic ondansetron and fluoxetine as one of a large number of possible combinations of 5-HT_3 antagonist and a 5-HT reuptake inhibitor, those of ordinary skill in the art would not have been motivated to specifically select these two agents and use them in a combination. This is because the combination of ondansetron and fluoxetine is merely one of numerous possible combinations disclosed in the '103 publication, and the '103 publication discloses nothing whatsoever regarding the desirability of that specific combination.

In this regard, the Examiner, citing *In re Petering*, disagrees with Applicants apparently because the '103 publication discloses "a small Markush Group of only 12 5-HT reuptake inhibitors that includes fluoxetine." (Office Action, page 2). Based on this allegation, the Examiner contends that it would have been obvious for those of ordinary skill in the art to select fluoxetine (among twelve 5-HT reuptake inhibitors recited by claim 7 of

the '103 publication) and ondansetron, in view of claim 2. (*Id.*). Applicants respectfully disagree.

Specifically, Applicants respectfully point out that the Examiner's allegation, particularly that the selection of ondansetron would have been obvious in view of claim 2 of the '103 publication, has no basis. This is because claim 2 of the '103 publication merely recites the combination of "5-HT_3 antagonist and a 5-HT reuptake inhibitor," without any limitations to the specific 5-HT_3 antagonists. Further, the '103 publication defines "5-HT_3 antagonist" by referring to ten different publications, which, in turn, disclose hundreds of compounds and refer to yet additional references that presumably disclose additional 5-HT_3 antagonists. Thus, literally thousands of combinations can result from the genii disclosed in claims 2 (hundreds of 5-HT_3 antagonists) and 7 (twelve 5-HT reuptake inhibitors) of the '103 reference - far greater than the 20 compound genus at issue in *Petering*.[1]

Thus, even assuming, *arguendo*, that claim 7 of the '103 publication somehow directs those of ordinary skill in the art to select fluoxetine, no motivation or suggestion to select ondansetron among hundreds of 5-HT_3 antagonists disclosed, and combine it with fluoxetine, would have been provided by the '103 publication (and claim 2 thereof), contrary to what the Examiner alleges. As well-settled, the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. (*Manual of Patent Examining Procedure* ("MPEP") § 2144.08; *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994); *see also In re Brouwer*, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996)(the mere fact that one species selected from a genus could be modified or replaced to reach the claimed invention does not render the claims obvious unless the prior art suggested that modification or replacement)).

Applicants further point out that the '302 patent does not cure the deficiency of the '103 publication because the '302 patent does not even remotely disclose or suggest that R(+) ondansetron can be used in combination with other agents.[2] Therefore, as the '103 publication does not provide any suggestion or motivation to select the combination of

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[1] In this regard, Applicants point out that a genus of 259 members, for example, has been held to be sufficiently large to avoid anticipation of a species. (*In re Ruschig*, 343 F.2d 965, 974-75, 145 USPQ 274, 282 (Fed. Cir. 1965)(comparing a genus of 259 compounds to the 20 member genus in *Petering*)).

[2] The Examiner appears to be in accord with Applicants regarding this point, as the Examiner clearly states that Young is "cited solely for the teaching of optically pure R(+) ondansetron." (Advisory Action, page 2). Thus, it is clear that Young would not have provided any motivation with respect to the combination of ondansetron and fluoxetine.

ondansetron and fluoxetine, and the '302 patent does not cure this deficiency, Applicants respectfully point out that the rejection under 35 U.S.C. § 103 cannot stand for this reason alone.

Second, Applicants respectfully submit that even assuming, *arguendo*, that those of ordinary skill in the art would somehow select the specific combination of ondansetron and fluoxetine, the references cited by the Examiner as a whole would not have motivated those skilled in the art to replace ondansetron with R(+) ondansetron, as recited by the pending claims. In this regard, Applicants note that the Examiner, relying on the disclosure of the '302 patent, that those skilled in the art would have been motivated to replace racemic ondansetron with R(+) ondansetron in this particular combination of ondansetron and fluoxetine, as disclosed by the '103 publication.[3] Applicants respectfully disagree.

The '103 publication states, in connection with the combinations disclosed therein, that "no adverse toxicological effects are indicated with the composition" disclosed therein. (The '103 publication, page 4, lines 10-12) (emphasis added). Therefore, regardless of what the '302 patent discloses, those skilled in the art reading the '103 publication would have had no reason to even look for a replacement of ondansetron. Therefore, the disclosure of the '302 patent relied on by the Examiner, when read in view of the disclosure of the '103 publication, could not have specifically motivated those of ordinary skill in the art to make and use the combination of R(+) ondansetron and fluoxetine. For this additional reason, Applicants respectfully submit that the rejection under 35 U.S.C. § 103 cannot stand.

In sum, Applicants respectfully point out that the claims are not obvious because neither the '103 publication, nor the '302 patent, provide any suggestion or motivation to arrive at the claimed invention. Therefore, Applicants respectfully submit that the rejection of the claims under 35 U.S.C. § 103 should be withdrawn.

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[3] Again, Applicants respectfully point out that the '103 publication does not even disclose or suggest the specific combination of ondansetron and fluoxetine, as discussed above.

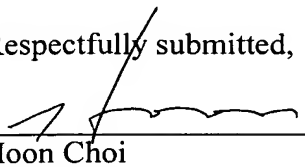
CONCLUSION

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and thus, request the withdrawal of the rejection thereof.

Please apply fees for the Extension of Time ($450.00) and filing fee for Request for Continued Examination ($790.00) and any other charges, or any credits, to Jones Day Deposit Account No. 503013.

Respectfully submitted,

Date: November 6, 2006



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